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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,504	07/31/2001	R. Martin Emanuele	19720-0625 (42896-261843)	3166

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	12

DATE MAILED: 10/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,504	EMANUELE ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cov r sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *17 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

An amendment was received and entered as Paper No. 10 on 7/17/03. Claims 39-42 were added as requested. Claims 1-42 are pending and under consideration in this Office Action.

Rejections Withdrawn

After further consideration, the rejection of claims 1-38 for lack of enablement and written description is withdrawn.

The rejections of claims 1-38 over 35 USC 112, second paragraph are withdrawn in view of Applicant's amendments, and replaced by new grounds of rejection necessitated by Applicant's amendments.

The rejections of claims 1-4, 9-12, 17-22, 27-30, and 33-36 under 35 U.S.C. 102(b) over Hunter et al (US Patent Nos. 5,234, 683, issued 8/10/93) and Jansen et al (US Patent 4,902,500, issued 2/20/90) are withdrawn in view of Applicant's amendments.

The rejection of claims 6, 7, 14, 15, 24, 25, 32, and 37 under 35 U.S.C. 103(a) as being unpatentable over Hunter et al (US Patent 5,234,683) is withdrawn in view of Applicant's amendments, and replaced by new grounds of rejection necessitated by Applicant's amendments.

Priority

Applicant has claimed priority under 35 USC 120 to a variety of US patent applications. This priority claim cannot be granted for the following reasons. All instant claims embrace compositions comprising an octablock copolymer and a nucleic acid, however none of the priority documents provides support for this combination of limitations. For this reason, the filing date of the instant claims must be the filing date of the instant application, 7/31/01.

Response to Arguments

Applicants arguments filed 10/5/03 have been fully considered but are unpersuasive.

Applicant argues that prior application 08/138,271 supports the instant invention because it discloses nucleic acids and, through reference to Schmolka (J. Am. Oil Chemist Soc. 54:110-116(1977) discloses octablock copolymers as well. A review of Schmolka shows that this reference teaches how to make poloxamers, meroxapols, poloxamines (i.e. octablock copolymers), and pluradot polyols. See Figs. 1-4. However, Applicant has failed to provide any evidence or logic to indicate that the '271 application relied upon Schmolka for its disclosure of octablock copolymers. A review of the specification of '271 reveals that the invention claimed therein was directed to admixtures of a therapeutic compound (e.g. a nucleic acid) and an effective amount of a block copolymer of the general formula:

$$HO(C_2H_4O)_bC_3H_6O)_a(C_2H_4O)_bH,$$

which is the general formula of a poloxamer. The specification of '271 does not appear to disclose or describe any copolymer other than a poloxamer, except by reference to Schmolka. The Schmolka reference is referred to at page 17, lines 12-18, as providing a description of how to prepare the copolymers represented in Fig. 1 of '271. Fig. 1 discloses 21 copolymers, 17 of which are products of BASF corporation having trade names beginning with a prefix 'L', 'P', or 'F'. BASF corporation uses the prefix 'T' to denote octablock copolymers, so none of these 17 copolymers appears to be an octablock copolymer. The remaining 4 copolymers are CRL 336, CRL 1190, CRL 1235, and CRL 8950. There is nothing in the specification to suggest that any of these compounds is an octablock copolymer, and Applicant has provided no evidence or argument indicating such. In view of the available evidence, one of skill in the art would consider the specification of '271 to be directed to poloxamers of the general formula:

$$HO(C_2H_4O)_bC_3H_6O)_a(C_2H_4O)_bH,$$

and would consider the reference to Schmolka as guidance for to how to make these poloxamers. In the absence of any disclosure of in the specification of '271 of octablock copolymers, one of skill in the art would not refer to Schmolka for guidance as to how to make these compounds.

Applicant points out that US Patents 5,990,241, 5,114,708, and 5,183,678 each describe octablock copolymers. This is true, but none of these documents discloses nucleic acids, so none of these documents discloses the combination of nucleic acids and octablock copolymers. As a result, these documents provides support for the instantly claimed invention.

For these reasons, the filing date of the instant claims must be the filing date of the instant application, 7/31/01.

Compliance with Sequence Rules

Applicant's submission of a CRF and paper copy of a Sequence Listing is acknowledged. The Examiner has amended the specification at page 30, line 31 to reflect that the disclosed oligonucleotide is SEQ ID NO:1. The Application is now in compliance with the Sequence Rules.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-38 are indefinite because the intended scope of the nucleic acids intended to be embraced is unclear. Specifically, it is unclear if Applicant intends to claim composition comprising oligonucleotides such antisense , triplex formers, and ribozymes, or whether Applicant intends to claim nucleic acid sequences encoding such oligonucleotides, e.g. expression vectors encoding antisense oligonucleotides.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 8-13, 16-23, 26-31, 33-36, and 38 stand rejected under 35 U.S.C. 102(e) as being anticipated by Lemieux et al (US Patent 6,359,054, issued 3/19/02).

Lemieux teaches methods of delivering to an animal a composition comprising octablock block copolymers and nucleic acids, (see e.g. claim 13 at column 49). The nucleic acid can be an expression vector, antisense, ribozyme, or oligonucleotide (see column 21, lines 15-29). The octablock copolymers useful in the invention include a variety of conventional and reverse orientation octablock copolymers set forth at column 15, lines 8-45 and 25-31, including Pluronics T1101, T1301, T1501 and T110R1, T130R1, and T150R1 (see column 14, lines 34-36 and 54-62). Pluronic T1501 corresponds to the octablock copolymer recited in instant claims 1, 2, and 17-20. Pluronic T1301 corresponds to the copolymer in instant claims 3 and 21. Pluronic T1101 corresponds to the copolymer in instant claims 4 and 22. Pluronic T150R1 corresponds to the copolymer in instant claims 9, 10, 27, 28, 33, and 34. Pluronic T130R1 corresponds to the copolymer in instant claims 11, 29, and 35. Pluronic T110R1 corresponds to the copolymer in instant claims 12, 30, and 36.

Thus Lemieux anticipates the claims.

Response to Arguments

Applicants arguments filed 10/5/03 have been fully considered but are unpersuasive. Applicant argues that Lemieux cannot be considered prior art because the effective filing date of the instant application is 10/15/93. This is unpersuasive for

the reasons set forth above under Priority, i.e. the effective filing date of the instant application is 7/31/01. Applicant's argument that Lemieux fails to meet the limitations of claims 2-4, 12, 18, 20-22, 30, and 36 is unsupported. Applicant has failed to state what limitations are not met and why., whereas the rejection above clearly shows which octablock copolymers of Lemieux correspond to the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 7, 9, 14, 15, 19, 24, 25, 27, 32, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Lemieux et al (US Patent 6,359,054, issued 3/19/02), and further in view of Emanuele (US Patent 5,656,611, issued 8/12/97).

Lemieux teaches methods of delivering to an animal a composition comprising emulsions of non-ionic block copolymers and nucleic acids. See e.g. claim 18. The copolymers are organized as octablocks (see e.g. claim 13 at column 49). The nucleic acid can be an expression vector, antisense, ribozyme, or oligonucleotide (see column 21, lines 15-29). The octablock copolymers useful in the invention include a variety of conventional and reverse orientation octablock copolymers set forth at column 15, lines 8-45 and 25-31, including Pluronics T1101, T1301, T1501 and T110R1, T130R1, and T150R1 (see column 14, lines 34-36 and 54-62). Pluronic T1501 corresponds to the

octablock copolymer recited in instant claims 1, 6, 7, 19, 24, and 25. Pluronic T150R1 corresponds to the copolymer in instant claims 27, 32, and 37. Lemieux also teaches that the compositions may comprises TWEEN as a surfactant. See column 20, lines 43-47.

Lemieux does not teach a composition comprising both 0.1-5% by weight of a surfactant and 0.5-5% by volume of a low molecular weight alcohol.

Emanuele teaches that surfactants such as polyoxyethylenesorbitan (20) monooleate (TWEEN 80), and low molecular weight alcohols such as ethanol may be added to emulsions of non-ionic block copolymer compositions comprising nucleic acids. See column 11, lines 39-58. Further, the ethanol may be in the concentration range of 0.5-5% by volume, and the surfactant may be in a range of approximately 0.1-5% by weight. See e.g. claims 3, 5, and 6.

It would have been obvious to one of ordinary skill in the art at the time of the invention to add the surfactants and low molecular weight alcohols of Emanuele to the compositions of Lemieux. One would have been motivated to do so in order to stabilize the emulsions.

Claims 1, 2, 5, 8, 17-20, 23, and 26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Pahlson et al (Acta Pathol. Microl. Immunol. Scand. B (1986) 94(3): 117-125), in view of Woodard (Laboratory Animal Science (1989 May) 39(3): 222-225).

Pahlson teaches a method of inducing an immune response in a mouse by administering whole bacteria emulsified in Freund's complete adjuvant. See abstract. Whole bacteria are considered to comprise expression vectors (chromosomes) comprising sequences (promoters) that can alter the function of nucleic acids (coding

sequences). Further, whole bacteria would also be considered to comprise ribozymes as part of their ribosomes, as well as antisense oligonucleotides (Okazaki fragments).

Pahlson does not teach an octablock copolymer.

Woodard teaches that the octablock copolymer T1501 is equivalent to Freund's complete adjuvant for the purpose of stimulating antibody production. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the T1501 octablock copolymer of Woodard for the Freund's complete adjuvant of Pahlson. One would have been motivated to do so because Woodard teaches that T1501 and Freund's complete adjuvant are equivalent in the art of stimulating antibody production. Regarding the obviousness of art-recognized equivalents, MPEP 2144.06 states in part:

> In order to rely on equivalence as a rationale supporting an obviousness rejection, the
> equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents... Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.).
>
> **An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious.** In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

Emphasis added. Because T1501 and Freund's complete adjuvant are art-recognized equivalents in stimulating antibody production, it would have been obvious to substitute one for the other, even in the absence of an express suggestion to do so.

Therefore the invention as a whole was *prima facie* obvious.

Claims 3, 4, 9-13, 16, 21, 22, 27-31, 33, 35, 36, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pahlson et al (Acta Pathol. Microl. Immunol. Scand. B (1986) 94(3): 117-125) and Woodard (Laboratory Animal Science (1989 May) 39(3): 222-225), as applied to claims 1, 2, 5, 8, 17-20, 23, and 26 above, and further in view of Jansen et al (US Patent 4,902,500, issued 2/20/90).

The teachings of Pahlson and Woodard are summarized above, and can be combined to render obvious compositions comprising an octablock copolymer of instant claims 1, 2, 5, 8, 17-20, 23, and 26, and nucleic acids such as expression constructs, ribozymes, and antisense oligonucleotides.

Pahlson and Woodard do not teach the octablock copolymers of instant claims 3, 4, 9-13, 16, 21, 22, 27-31, 33, 35, 36, and 38.

Jansen teaches the following octablock copolymers:

Pluronic T1301, corresponding to the copolymer in instant claims 3 and 21.

Pluronic T1101 corresponding to the copolymer in instant claims 4 and 22.

Pluronic T150R1 corresponding to the copolymer in instant claims 9, 10, 13, 16, 27, 28, 31, 33, and 38.

Pluronic T130R1 corresponding to the copolymer in instant claims 11, 29, and

Pluronic T110R1 corresponding to the copolymer in instant claims 12, 30, and

It would also have been obvious to substitute the T1301, T1101, T150R1, T130R2, and T110R1 of Jansen for Freund's complete adjuvant in the invention of Pahlson. One would have been motivated to do so because these compounds have very close structural similarities to T1501, which is an art recognized functional equivalent of Freund's complete adjuvant, and would reasonably be expected to have similar performance characteristics.

Therefore the invention as a whole was *prima facie* obvious.

Claims 1-5, 8-13, 16-18, 20-22, 28-30, and 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kabanov et al (US Patent 5,656,611, issued 8/12/97).

Kabanov teaches compositions comprising polynucleotides and octablock copolymers having molecular weights and relative amounts of POP and POE overlapping those of the instant claims. See abstract and column 7, line 23 to column 8, line 11, especially column 7, lines 40-50). The polynucleotides may be antisense, oligonucleotides, ribozymes, or expression vectors (see column 10, lines 9-28. The copolymers may be of standard or reversed orientation (see column 7, line 64 to column 8, line 3). The compositions of the copolymers, with respect to the amounts and proportions of POE and POP, embrace a wide variety of compounds (see e.g. column 7, lines 48-51 which disclose that POP and POE monomers may be present in each of the four octablock copolymers in amounts of from about 5 to about 400 monomers).

Kabanov does not teach the precise limitations of the claims with respect to the molecular weight of the POP portion of the copolymer, or the relative amounts of POP and POE in the copolymers. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to arrive at the compositions set forth in the claims in the process of optimizing the invention of Kabanov for the disclosed purpose of delivering nucleic acids to cells. Because the Kabanov teaches a range of compositions which overlaps or embraces those of the instant invention, Kabanov teaches the general conditions of the claims. "[W]here the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Thus the invention as a whole was *prima facie* obvious.

Response to Arguments

Applicants arguments filed 10/5/03 have been fully considered but are unpersuasive.

With respect to the rejections based on Pahlson and Woodard, Applicant argues at page 33 of the response that these references fail to teach compositions comprising isolated or amplified nucleic acid sequences encoding gene products, oligonucleotides, antisense oligonucleotides, triplex DNA compounds or ribozymes. In response, the PTO notes that the specification does not define the newly-introduced phrase "isolated or amplified nucleic acid sequences", so it has been given its broadest reasonable interpretation. For example, the compositions of Pahlson are considered to comprise amplified nucleic acids because the bacteria comprising the nucleic acids were amplified in culture (i.e. grown in culture), see page 118, column 1, second full paragraph. For these reasons the rejection is maintained.

With respect to the rejection based on Kabanov, Applicant argues at page 34 of th4e response that Kabanov cannot be considered prior art because the effective filing date of the instant application is 10/15/93. This is unpersuasive for the reasons set forth above under Priority, i.e. the effective filing date of the instant application is 7/31/01.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the

application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER